REMARKS

Applicants appreciate the examination of the present application as evidenced by the Office Action dated June 16, 2010 (hereinafter, "the Office Action"). Upon entry of this Amendment, Claims 1, 3, 6-10, 12-16, 25, 28 and 31-39 are pending in the present application, and these claims stand rejected.

In view of the foregoing amendments and following remarks to address the issues raised in the Office Action, reconsideration and withdrawal of the rejections to the present application are respectfully requested, and favorable action upon all pending claims is hereby requested.

I. Claim Rejections Under 35 U.S.C. §103

Claims 1, 3, 6-10, 12-16, 25, 28 and 31-39 stand rejected under 35 U.S.C. §103(a) as being unpatentable over U.S. Patent No. 6,407,212 B1 to Morgenhalter et al. (hereinafter, "Morgenhalter") in view of U.S. Patent No. 6,083,408 to Breitenbach et al. ("Breitenbach"). *See* Office Action, page 3.

First, Applicants respectfully question whether Morgenhalter should be considered "prior art." Applicants note that the qualifying date for Morgenhalter under 35 U.S.C. § 102(a) is believed to be August 19, 1999, and the qualifying date under 35 U.S.C. § 102(e) is believed to be July 28, 2000. However, the present application claims priority to, for example, prior filed British Application GB9910476.2 filed May 7, 1999. In the event that the Examiner maintains that Morgenhalter is prior art, Applicants respectfully submit that Morgenhalter alone, or in combination with Breitenbach, fails to render the pending claims obvious.

The Office Action states the following:

> It is noted that while Morgenhalter does not expressly call his filter a depth filter, it is the position of the Office that Morgenhalter's filter is a depth filter since it is composed of identical components, (kieselguhr, perlite and cellulose) and it is used for the same purpose, removing submicron contaminants from human blood plasma as the depth filter disclosed in Breitenbach.
>
> However, it would have been *prima facie* obvious to provide the Breitenbach's filter in the method of Morgenhalter because Breitenbach teaches that his filter can successfully pass human blood plasma products while removing contaminants such as viruses.

Office Action, page 4 (citations omitted).

Regarding Morgenthaler, in column 3, this reference describes the noted difficulties relating to the removal of abnormal prion proteins (NCTAs) from donated blood or plasma. In column 3, starting at line 34, Morgenthaler emphasizes that prion proteins are uncommonly stable against inactivation and that known methods for the inactivation of viruses do not diminish the infectivity of NCTAs. Conditions known to reliably inactivate NCTAs are at least as effective at inactivating the human plasma proteins themselves. Morgenthaler concludes (*see* column 3, line 46) that the only alternative appears to be physical removal of the NCTAs. The reference asserts, "[s]ince the monomers of the infectious compounds may be of similar size as human plasma proteins, they cannot easily be removed by, e.g. (nano)filtration or centrifugation. It has indeed been shown that nanofiltration was able to remove NCTAs but that the removal depended on the presence or absence of certain solutes; e.g. the infectious agents passed through the filter in the presence of surfactants." Morgenthaler, column 3, lines 48-53.

Thus, there is a very clear teaching in Morgenthaler that filtration is not a promising route for the removal of abnormal prion proteins from solutions of blood plasma proteins. As noted in Applicant's previous response submitted March 8, 2010, nanofiltration would not only remove the prion proteins but would also remove the blood plasma proteins themselves. Morgenthaler is quite clearly stating that since abnormal prion proteins and blood plasma proteins are of a similar size, filtration could not be expected to be effective. This is a clear teaching away from the use of depth filters, as used in the methods of the present invention.

Morgenthaler's solution to the problem is whereby NCTAs which may be present in protein solutions are to be absorbed on certain materials including kieselguhr and perlite (*see* column 3, line 66). At column 4, lines 2-6, Morgenthaler states:

> If the protein solutions are brought in contact with these materials for a sufficiently long time, the separation of a solution into a precipitate and a supernatant therefore results in further removal of NCTAs in addition to the removal effected by the precipitation step per se.

Thus, Morgenthaler emphasizes that the protein solutions should be brought into contact with the liquid for a sufficiently long time for adsorption to occur. There is no teaching or suggestion of forming the materials into a solid depth filter including a binder, as recited in the pending claims. Indeed, the whole of the Morgenthaler disclosure is that the adsorbent should be effectively loose or suspended in solution. That same paragraph continues to state that the

adsorptive materials may already be present in the solution from being used in previous fractionation steps as filter aids - in order to facilitate the separation of the precipitate and the supernatant during ethanol fractionation. Applicants note, however, that conventional blood plasma fractionation technology involves various freezing and thawing steps in the presence of cold ethanol and the "precipitate" referred to there is the solid blood plasma protein material which forms as part of the freeze-thaw cycle. So in effect, Morgenthaler is using "precipitate" in two senses. First, it refers to the production of a semi-solid precipitate of blood plasma proteins during the freeze-thaw cycles. Second, the term "precipitate" refers to the particulate adsorptive material on which prion proteins have been adsorbed.

Morgenthaler further states in column 4, lines 18 and 19 that "NCTAs are removed from the protein solution by absorption on a solid phase." That solid phase is normally particulate material suspended in solution or alternatively the particulate absorptive materials may have already been "formed before hand on a porous filter." Column 4, lines 22 and 23. However, there is no disclosure or suggestion that the blood plasma protein solution is passed through the filter, merely that the particulates are deposited on top of the filter in the manner of a filter aid. Indeed, the entirety of Morgenthaler is contrary to the passing of blood plasma solutions through the filter, because this would not allow the long absorption times taught by Morgenthaler.

The "filter aid" referred to by Morgenthaler is distinguishable from the solid depth filter of the pending claims. Filter aid refers to loose particles, which are provided as a loose layer on a filter. The filter aid material does not function as a filter itself, but merely provides a barrier to prevent fouling of the filter by particulates (*see also* Morgenthaler, column 4, line 10). On the contrary, the depth filter recited in the pending claims is instead a solid matrix of particles including a binder and bonded together by a resin.

Contrary to the assertions of the Office Action, Morgenthaler does not teach a method of removing prions from plasma products by passing the blood plasma products through a filter formed of a cellulose binder and kieselguhr or perlite particles. Morgenthaler nowhere teaches or suggests passing the blood plasma product through a filter. Again, this would not provide the extended absorption times noted by the Morgenthaler process. Moreover, Morgenthaler does not disclose or suggest the use of a solid depth filter including a binder. Morgenthaler instead employs loose particulate absorptive material, which is brought in contact with the blood plasma protein solution.

In summary, there are clear differences between embodiments of the present invention and Morgenthaler such as the following:

1. Embodiments of the present invention employ a solid depth filter matrix including a binder; whereas Morgenthaler utilizes loose particular material, either in suspension or deposited as a layer on a filter.

2. Embodiments of the present invention are directed to passing a blood plasma protein solution through the filter in order to remove abnormal prion proteins. In contrast, Morgenthaler simply contacts the solution with the particulate absorbent and nowhere discloses or suggests filtration.

3. It is surprising that the filter embodying aspects of the present invention will retain prion protein but pass blood plasma proteins of interest, even with pore sizes normally expected to allow free passage of both prion protein and protein of interest. *See* the filtration schematic submitted with Applicant's response submitted March 8, 2010.

4. Embodiments of the present invention do not utilize denaturing conditions, which could potentially degrade the blood plasma protein of interest.

5. In embodiments of the present invention, prion protein is removed below detectable levels, not merely reduced yet still detectable.

6. The Morgenthaler process utilizes subsequent separation (by filtration or centrifugation) of the particulate suspension from the solution; whereas the use of the solid depth filter matrix according to embodiments of the present invention avoids this necessity– Thereby contributing not only to the medical/scientific value of the present invention, but also to its commercial value.

Breitebach fails to cure the deficiencies of Morgenthaler. More specifically, Breitenbach does indeed disclose the use of a depth filter, but it is not a depth filter formed of kieselguhr and perlite. Kieselguhr is used as a comparison in Example 2 of Breitenbach, where unfavorable conclusions are drawn. Instead, materials used in Breitenbach are biocidal and viricidal but this is by virtue of the iodine biocidal compounds (crospovidone-iodine) which are incorporated in the filters. Thus, column 4, line 43 asserts that bacteria, fungi or viruses are killed or inactivated by the iodine compound present. There is no teaching or suggestion that this is due to action of the depth filter itself, as in the pending claims.

Thus, while Breitenbach does describe the use of depth filters to remove bacteria, fungi

or viruses, this is by virtue of the iodine compounds present rather than the nature of the depth filter itself. There is no mention or suggestion of removal of abnormal prion proteins.

Moreover, there is no motivation for one of ordinary skill in the art to combine Morgenthaler and Breitenbach. The entire disclosure of Morgenthaler is that extended contact times are required in order to achieve complete prion removal. Using the solid depth filter taught by Breitenbach would tend to give shorter contact times because the liquid is only in contact with the adsorptive material for the short time during which the liquid is passing through the filter. Thus, the entire teaching of Morgenthaler teaches away from the use of short contact time depth filters. Further, Breitenbach teaches the need to include an iodine biocidal compound in order to deactivate the contaminants. The presence of such biocidal compounds could not be tolerated in pharmaceutical blood plasma products. For at least these reasons, one of ordinary skill in the art would be deterred from combining Morgenthaler with Breitenbach.

Accordingly, Applicants respectfully request that the rejection of claims 1, 3, 6-10, 12-16, 25, 28 and 31-39 under 35 U.S.C. §103(a) be withdrawn.

II. Claim Rejections Under35 U.S.C. §101

Claim 14 stands rejected under 35 U.S.C. §101 because the claimed invention is allegedly directed to a non-statutory subject matter. *See* Office Action, page 5. Applicants have amended claim 14 to refer to the resulting transformed product that is not a product of nature, but a product resulting from being subjected to the method recited in claim 1. Accordingly, Applicants respectfully request that this rejection be withdrawn.

III. Double Patenting Warning

The Office Action indicates that should claim 1 be found allowable, claim 31 will be objected to as being a substantial duplicate thereof. *See* Office Action, page 5. Applicants respectfully request reconsideration of this position, and Applicants will resolve any outstanding issue regarding these claims as appropriate.

CONCLUSION

Accordingly, Applicants submit that the present application is in condition for allowance and the same is earnestly solicited. The Examiner is encouraged to telephone the undersigned at 919-854-1400 for resolution of any outstanding issues.

Respectfully submitted,

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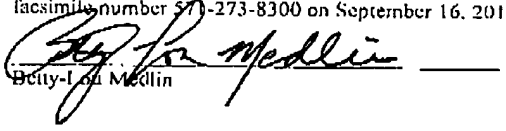

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